

Amendments to the Claims

Claims 1-77 (cancelled)

Claim 78 (currently amended): A composition for detecting the effect of an enzyme on a peptide substrate, the activity of said enzyme ~~activity~~ being effective to convert said peptide substrate from an unmodified state to a modified state ~~while leaving said substrate otherwise intact~~, said composition comprising a functional peptide substrate ~~or functional fragment thereof~~ for said enzyme, having a first detectable proximity-sensor peptide incorporated into a first position of said substrate and a second detectable proximity-sensor peptide incorporated into a second position of said substrate, thereby providing a semi-synthetic multiple labeled polypeptide substrate having a first structural conformation in said unmodified state and a second structural conformation in said modified state, said proximity sensors being spaced apart in said first structural conformation at a distance which is characteristic of said unmodified state and being spaced apart in said second structural conformation at a distance which is characteristic of said modified state, detection of one of said structural conformations being indicative of the effect of said enzyme on said substrate.

Claim 79 (original): The composition of claim 78, wherein said enzyme a kinase.

Claim 80 (original): The composition of claim 79, wherein said kinase is Abelson protein tyrosine kinase.

Claim 81 (original): The composition of claim 78, wherein said peptide substrate is Crk-II.

Claim 82 (original): The composition of claim 78, wherein said modification of said substrate is a post-translational

modification.

Claim 83 (original): The composition of claim 82, wherein said modification of said substrate is a phosphorylation modification.

Claim 84 (original): The composition of claim 82, wherein said modification of said substrate is a dephosphorylation modification.

Claim 85 (original): The composition of claim 78, further comprising a modulator of said enzyme.

Claim 86 (original): The composition of claim 85, wherein said modulator of said enzyme inhibits said enzyme activity.

Claim 87 (original): The composition of claim 85, wherein said modulator of said enzyme activates said enzyme activity.

Claim 88 (original): The composition of claim 78 wherein said first detectable proximity-sensor peptide is at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said semi-synthetic multiple labeled polypeptide, the C-terminus of which is peptide bonded to the N-terminus of said second detectable proximity-sensor peptide.

Claim 89 (currently amended): The composition of claim 78 wherein said substrate ~~enzyme~~ is a recombinant polypeptide.

Claim 90 (original): The composition of claim 78 wherein said first and second detectable proximity-sensor peptides of said semi-synthetic multiple labeled polypeptide comprise a FRET pair.

Claim 91 (original): The composition of claim 90 wherein said

FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and fluorescein, EDANS and DABCYL, BODIPY fluorescein and BODIPY FL fluorescein, β -phycoerythrin and CY5, and pyrene and coumarin.

Claim 92 (original): The composition of claim 90, wherein said FRET pair comprises fluorescein and tetramethylrhodamine.

Claim 93 (original): The composition of claim 78 wherein said detectable proximity-sensor peptide is a synthetic oligopeptide comprising a fluorescent amino acid derivative.

Claim 94 (original): The composition of claim 78 as set forth in Figure 5A (SEQ ID NO: 8).

Claim 95 (original): The composition as shown in SEQ ID NO: 9.